LABORATORY

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Office Techniques for Dermatologic Diagnosis

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Although many skin diseases may be quickly recognized by their characteristic clinical appearance, simple diagnostic procedures readily provide confirmation of a first impression. These may generally be performed at the bedside or in an office and are often the definitive method of differentiating between morphologically similar skin problems. The importance of developing skill in performing these diagnostic techniques should not be minimized, for even experienced dermatologists routinely confirm a diagnostic impression with a microscopic evaluation and are prepared to consider a working diagnosis on the basis of these tests.

Manipulative Techniques

DEFINITION

Performed at the bedside with no tool more complex than the physician's fingertip, the manipulative techniques are helpful adjuncts to dermatologic diagnosis.

Diascopy

This technique is a more sophisticated modification of the simplest method for assessing superficial erythema: pressing the fingertip against the skin and withdrawing it quickly to see if blanching occurs. Diascopy is a refinement in which a piece of clear glass or plastic is pressed against the skin while the observer looks directly at the lesion under pressure. The purpose of this procedure is to empty blood from the superficial vessels to determine if skin redness is due to blood within vessels (erythema) or extravasated into the skin (petechiae, purpura). The former will blanch with pressure, the latter will not. By varying the pressure on the skin, vessels can be seen to blanch and fill. The amount of pressure required to blanch a given lesion is variable, but care should be exercised when using a glass microscope slide, lest a sharp edge damage the skin or the slide break under pressure and lacerate the skin. It is probably best to use two glass slides together to minimize this risk.

CLINICAL SIGNIFICANCE

Specific indications for the use of diascopy include: telangiectasia (in which the central "feeder" vessel may be distinguished); petechiae and purpura; superficially dilated veins (venous lake, varicosities); and granulomatous nodules such as sarcoidosis, granuloma annulare, and lupus vulgaris (all three of which will reveal a brownish-yellow "apple jelly" translucent quality upon diascopy).

Dermatographism

The whealing or urticarial response of the skin produced when it is stroked firmly with a pointed object is known as dermatographism ("skin writing"). This phenomenon may be elicited in up to 50% of normal people with firm stroking and is an exaggeration of the physiologic triple response of Lewis. The diagnosis of dermatographism is given only to those few individuals who manifest an urticarial response to mild physical trauma.

CLINICAL SIGNIFICANCE

The significance of dermatographism is primarily its ability to reproduce the lesions of which the patient complains. It is classified as a form of physical urticaria and is not actually more common in people with chronic urticaria than in other people. Interestingly, it has been reported that up to 75% of pregnant women may have dermatographism, and the wheal response may also be elicited with urticaria pigmentosa (see Darier's sign, below).

Darier's Sign

Similar to dermatographism, this sign refers to the wheal or hive produced by rubbing a flat, tan macule of urticaria pigmentosa.

CLINICAL SIGNIFICANCE

Lesions of urticaria pigmentosa contain excessive numbers of mast cells, which release histamine in response to trauma and cause the skin to urticate. Lesions of urticaria pigmentosa in children may even blister when traumatized, and a solitary mastocytoma may also give this response. Although Darier's sign is virtually diagnostic of urticaria pigmentosa, failure to elicit this sign does not necessarily exclude the diagnosis.

Nikolsky's Sign

This sign is elicited in blistering diseases to determine whether the epidermis is adherent to the underlying dermis. A finger or rounded object such as a pencil eraser is used to rub or rotate the skin with a mild shearing effect.

CLINICAL SIGNIFICANCE

One should suspect disadherence in the presence of large blisters, large areas of erosion and crusting, and areas of nonblanchable red skin. Diagnostic possibilities include pemphigus and toxic epidermal necrolysis due to staphylococcal scalded skin syndrome. Nikolsky's sign is most easily produced when the epidermis is acantholytic, a condition in which the epidermal cells lose attachment to one another. This sign is not diagnostic or absolutely specific, for it may be seen in severe cases of erythema multiformae, epidermolysis bullosa, pemphigoid, and variegate porphyria.

Auspitz Sign

When the thick white scale of psoriasis is carefully scraped away from the surface of a plaque, tiny bleeding points may be seen in the underlying epidermis.

CLINICAL SIGNIFICANCE

These points are the vascular dermal papillae that have been traumatized by removal of the thin suprapapillary epidermis. It is typical, but not diagnostic, of psoriasis.

Wood's Light Evaluation

DEFINITION

Probably most useful to the dermatologist, the 360 mm "black light" aids in diagnosis by causing certain skin lesions to fluoresce.

TECHNIQUE

It is necessary to warm up the Wood's lamp for several minutes before the examination to ensure optimum light intensity. The room should be dark, and the examiner should allow sufficient time for his eyes to adapt before conducting the skin examination. The light is not harmful to the skin and eyes, and the patient should be reassured. The optimum distance for the lamp from the skin is approximately 10 to 12 cm. Holding the lamp closer than this can give an artificial red-purple reflection, especially on black skin.

CLINICAL SIGNIFICANCE

In certain climates, erythrasma is seen as a nonspecific scaly groin eruption. The Wood's light causes this infection to glow with a characteristic coral red color. (Normal Corynebacterium in follicular orifices on the face will also show this coral red fluorescence.) Pseudomonas takes on a pale blue color, making this examination useful in evaluating secondary skin infection in such clinical situations as burn wounds. White macules of vitiligo may be accentuated with the Wood's light, and certain tinea infections are also fluorescent. The Wood's lamp was at one time a useful screening examination for tinea capitis in school children, but unfortunately Microsporum strains, which fluoresce most brightly, are no longer the most common causative organisms in this population. When the diagnosis of porphyria cutanea tarda is suspected, the patient's urine may be examined with the Wood's lamp for the characteristic pink to pink-orange fluorescence. Systemic tetracycline therapy causes the urine to fluoresce yellow, and this may be used to confirm that patients are actually taking the prescribed medication.

Microscopic Evaluation

DEFINITION

A simple light microscope with a $10 \times$ and $40 \times$ objective is sufficient for most dermatologic office evaluations.

Potassium Hydroxide

DEFINITION

Used for examining areas of the stratum corneum for evidence of superficial fungal disease (dermatophytosis), the

potassium hydroxide (KOH) examination is the diagnostic test most commonly performed in the dermatologist's office. The alkaline KOH solution separates and eventually destroys cells of the stratum corneum, permitting the hyphae and spores of dermatophytes to become more clearly visible. A 10 to 20% KOH solution is most commonly employed.

TECHNIQUE

The lesion border should be gently scraped with a scalpel or the edge of a microscope slide and flakes collected on a piece of paper or another glass slide. Only the superficial scale is required, and no blood should be drawn in the scraping process. If blisters are present, the blister roof should be trimmed off with scissors and placed on the microscope slide. A drop or two of KOH solution is then added to the specimen, and a coverslip is applied. For thick specimens, gentle heat will hasten the dissolution of the epidermis. This should be done gently, as drying the KOH may cause crystal formation, which makes identification of hyphae more difficult.

Fungal hyphae are cylindrical, uniform in diameter, and branched. Irregular "thick and thin" strands are probably artifacts, and epithelial cell borders can resemble branched hyphae unless the microscope is focused up and down during observation. Racking the slide condenser down to its lowest position and decreasing the light intensity are extremely helpful for accentuating the refractile quality of hyphal elements.

Although cutaneous Candida may also be diagnosed on a KOH preparation, it may be necessary to gram stain a pustule to observe gram-positive budding spore formation. In evaluating nail lesions, scales should be collected from white patches on the nail surface, from beneath the nail plate, or from the crumbling nail itself. In suspected tinea capitis, scales should be scraped from the scalp, and short broken hairs should be pulled out for examination.

CLINICAL SIGNIFICANCE

A negative KOH examination in the presence of strongly suspected fungal infection may be due to poor technique in examination of the specimen. It may be necessary to repeat the KOH examination with more material obtained from a more appropriate site. It is also important to allow sufficient time for the specimen to "clear" and to examine the entire specimen under the microscope. Sometimes gently pressing on the coverslip with a toothpick will flatten the specimen and enable one to distinguish between artifact and genuine dermatophyte. By consistently performing KOH examinations in cases of even "classic" tinea infection, the clinician will develop expertise in this technique.

Mineral Oil Preparation

DEFINITION

Primarily used for demonstration of ectoparasites such as scabies or lice, the mineral oil is used primarily as a vehicle to facilitate collection and hold the organism in place under the microscope.

TECHNIQUE

The diagnosis of scabies is suspected because of the appearance of 5- to 10-mm-long tracks or burrows on finger-

webs, wrists, or genitalia. A drop of immersion oil is placed on a microscope slide, and the scalpel blade is dipped into the oil before scraping the stratum corneum off the surface of the lesion. This oil makes it easier to collect the debris dislodged by the blade and keeps the specimen intact. Numerous lesions should be scraped and placed on the same microscope slide. Since good technique requires the examination of the entire specimen under the coverslip, the more material that is included, the higher the chance for success.

CLINICAL SIGNIFICANCE

Under the microscope, one will see the adult female mite (Sarcoptes scabiei), which is approximately 0.3 to 0.4 mm in diameter. There are four pairs of legs with bristles and spines on the dorsal surface of the back. Eggs are transparent and oval and of uniform size, approximately 0.1 to 0.15 mm. (Air bubbles may be mistaken for eggs, but the former are round and variable in size and will expand when the coverslip is pressed from above.) Scabies mites are almost always found intact, and the diagnosis should not be made by identification of supposed "legs" in the absence of other positive findings. Mite feces are reddish-brown irregular clumps, much smaller than eggs. They are usually found in association with mites and/or eggs.

Lice or pediculosis (capitis, corporis, pubis) may be seen with the naked eye in most cases, but to examine these ectoparasites under the microscope, they should be picked up with a forceps and placed on a drop of immersion oil on a microscope slide. Nits, which are generally found as tiny white attachments to hairs, are best examined by placing the hair itself with the attached nit in oil on a microscope slide.

Tzanck Smear

DEFINITION

The Tzanck smear is a means of determining the etiology of certain cutaneous blisters by observing epithelial cells from the blister base.

TECHNIQUE

This test requires removal of a fresh blister roof with iris scissors and/or forceps. The blister base thus exposed is scraped with the rounded portion of a scalpel blade and the specimen smeared on a microscope slide. The air-dried material is then stained with Wright's, Giemsa, PMS, or Sedistain. When the stain has dried, a drop of oil is then placed on the slide to enhance resolution, and the preparation is examined with a light microscope under $10 \times$ or $40 \times$ magnification.

CLINICAL SIGNIFICANCE

The Tzanck smear is useful in examining cells from blistering conditions. For the nondermatologist, it is of most diagnostic value in diagnosing herpes virus infections (both simplex and varicella-zoster). Epidermal cells are two to three times larger than polymorphonuclear leukocytes. Multinucleate giant cells, characteristically found in herpes virus infections, are far larger than epidermal cells. They contain many large nuclei within one cell or cytoplasmic compartment and may be easily seen at low magnification.

Other Diagnostic Tests

In some cases, it is not possible to obtain the answer to a diagnostic question while the patient is still in the office. Some tests take time to perform and interpret, but are nonetheless valuable for the specific information they convey to the physician.

Cultures

DEFINITION

The isolation and identification of microorganisms is a familiar diagnostic maneuver to the physician. Most of the time the term culture refers to bacteriologic testing. In dermatologic problems, however, the possibility of viral or fungal infection should be considered. Both of the latter conditions may cause inflammation of the skin with resultant pustules and blisters. Likewise, dermatitis of noninfectious etiology may easily become secondarily infected with Streptococcus and Staphylococcus, making the results of a bacterial culture less helpful in diagnosis than it might be in a primarily infectious process. Fortunately, viral cultures have become readily obtainable on a routine basis, often confirming a diagnosis of herpes simplex in a matter of days. This is particularly important in immunosuppressed patients, in whom herpes infections may smolder indefinitely or generalize to other areas of the body.

TECHNIQUE

Specific culture media are utilized for viruses and certain bacteria (e.g., anaerobes, acid-fast organisms), so it may be necessary to confirm with the hospital laboratory that the correct medium is being used for the organism sought. Typically, the wound is swabbed or probed with a cotton-tipped applicator that is then inserted into a tube containing an appropriate holding solution. Read the instructions carefully to be sure the material is handled correctly, and be especially careful to keep the culture material at the appropriate temperature (e.g., ice for viral cultures). The culture should be sent to the laboratory as soon as possible for processing.

The techniques for obtaining specimens for dermatophyte culture and for KOH examination are the same. A generous sample of scales and/or blister roof should be taken for implantation on appropriate dermatophyte medium. Hospital and/or diagnostic laboratories can identify fungi for nondermatologists culturing these organisms from the skin. Candida species can generally be identified in a few days, but fungal cultures may take up to 3 weeks for the characteristic morphology to become apparent.

Skin Biopsy

DEFINITION

Histologic sections of cutaneous tissue can be evaluated by the (dermato)pathologist for additional clinical information. Biopsies are especially important in diagnosing malignancies, but specimens may also be stained specifically to enhance the visualization of fungi or immune complexes.

TECHNIQUE

The technique of performing a punch or incisional biopsy of the skin is not a difficult one in itself, for the real expertise required is in the decision of which lesion(s) will give the most diagnostic appearance histologically. The general rule is to pick a fresh primary lesion for evaluation, bearing in mind that the histopathologic findings may be nonspecific in nature and should not be thought of as providing the ultimate answer in diagnosing the patient's condition. If a malignancy such as melanoma is suspected, the lesion should ideally be excised in toto. A superficial "shave" biopsy should not be performed if the depth of the lesion is the key to its prognosis and management. When in doubt, the patient should be referred to a specialist who is prepared to deal with the consequences of the patient's diagnosis and therapy.

Skin biopsies for immunofluorescence are especially helpful in the vesiculobullous disorders and lupus erythematosus. Tissue obtained for this test requires a special fixation medium, which should be obtainable from the laboratory reading the results of the immunofluorescence study. This special laboratory will be pleased to assist with advice on appropriate areas to biopsy, as nonlesional skin is preferred.

Patch Testing

DEFINITION

A test of cell-mediated immunity, patch testing is a means of determining whether a patient has a contact sensitivity to a given allergen. It should be distinguished from "scratch tests," which are performed by allergists and are a test of immediate or humoral immunity.

TECHNIQUE

In patch testing, a suspected antigen is fixed to the skin for a period of 48 hours, after which the patch is removed and the skin examined for evidence of erythema, induration, or blistering. The test is read again at 96 hours for delayed reactivity. Substances employed for patch testing are mixed to specific concentrations and formulas that have been developed for maximum efficacy and standardization. Although simple "use tests" may be performed by having the patient apply a potentially offending substance to an area on the inside of the upper arm daily for a period of 3 days, it is unwise to place potentially irritating substances on the skin and occlude them with tape for 48 hours. An irritant reaction is not necessarily an allergic one, and the test must be performed in a controlled fashion for it to have clinical relevance. This is particularly important in occupationally related dermatoses, in which Workman's Compensation litigation may result. It is probably best to seek the advice of a specialist in evaluations of this type.

Reference

Eaglstein WE, Pariser DM. Office techniques for diagnosing skin disease. Chicago: Year Book Medical Publishers, 1978.